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DIAGNOSTIC NEODYMIUM(III), YTTERBIUM(III), OR ERBIUM(III) ION-LIGAND COMPLEXES

Background of the Invention

The invention pertains to lanthanide ion-ligand complexes, in particular to neodymium(III) ion (Nd^{3+}), ytterbium(III) ion (Yb^{3+}), or erbium(III) ion (Er^{3+}) ligand complexes, to the use of said lanthanide ion-ligand complexes for the manufacture of a diagnostic kit, to a diagnostic kit comprising the same, and to a method of detecting an analyte in a matrix of biomedical interest.

The use of metal chelates as luminescent probes is well-known in the art, and the use of such probes for diagnostic purposes has recently been commercialized, while the state of the art of the technique has been reviewed by P.G. Sammes and G. Yahioglu in Natural Product Reports, Vol. 13, pp. 1-28 (1996). Europium and terbium ions (Eu(III) and Tb(III), respectively), both members of the rare-earth lanthanide metals, are very suitable as luminescent probes because of their long-lived luminescence, which allows for interference-free detection. By using a time delay between excitation pulse and detection optimized for the rare-earth ion, short-lived scatter and background luminescence from the matrix can be effectively removed. Since the absorption coefficients of rare-earth ions are extremely low (1-10 $l.mole^{-1}.cm^{-1}$) direct excitation is very inefficient. In general, excitation therefore requires the aid of a chromophore as sensitizer. For Tb(III) and Eu(III) ions, which emit in the visible part of the spectrum, sensitizers requiring UV excitation have to be applied as a result of energy constraints (the triplet state of the sensitizer should be at least 1000 cm^{-1} above the accepting state of the lanthanide ion). The other lanthanides in chelated forms in solution which exhibit luminescence in the visible part of the spectrum are gadolinium, samarium, and dysprosium ions. The other members of the lanthanide metals are considered to be unsuitable as luminescent probes because they have much smaller gaps between the

These lanthanide ion-ligand complexes further comprise an (immuno)-reactant for attachment to an analyte.

When the ligand is in contact with the sensitizing moiety, it may be covalently or ionogenically bonded, or the ligand may be in such close vicinity to the sensitizing moiety that energy transfer between the lanthanide ion-ligand complex and the sensitizing moiety is possible.

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Description of The Preferred Embodiments

These lanthanide ion-complexes can make use of inexpensive 400-1000 nm lasers or other light sources, emit luminescence in the near-IR spectrum, have long luminescence lifetimes, high sensitivity, and good stability with respect to the irradiated light and towards the solvents used, especially towards aqueous solutions.

More specifically, the lanthanide ion-complexes according to this invention have long luminescence lifetimes and do emit in the near-IR spectrum, which leads to "zero-interference" detection (necessary for diagnostic purposes). Further, the lanthanide ion-complexes according to this invention very efficiently quench the excited triplet state of the sensitizer, which is a major source of singlet oxygen leading to photo-oxidative damage, and therefore enhance stability.

In this respect luminescence is light which is emitted by a compound upon excitation by any means, among them irradiation of laser light.

Luminescence lifetime is the time in which the luminescence emission intensity has decayed to 1/e of its original value.

Luminescence quenching is the process which leads to radiationless deactivation of the luminescent excited state, for instance, as a result of collisions of the excited molecules with species which accept energy from the excited state and dispose of it non-radiatively.